IN THE DRAWINGS

Attached are corrected drawing sheets which are amended replacement drawings for the drawings of record. Please take note that Figs. 1 - 3 have been amended by including SEQ ID NOs. for the sequences therein. The corrected drawing sheets are labeled “Replacement Sheet”.

REMARKS

In the previous response, Applicant elected Group I covering claims 1-9 for further examination on the merits. Claims 10-26 have been withdrawn. However, by virtue of the Preliminary Amendment filed concurrently with the filing of the application on July 3, 2003, the subject application included 50 claims, not 26 claims. Claims 27-32 are believed to be clearly within the elected Group 1 and are assumed to be subject to examination on the merits pursuant to the Restriction Requirement. The Examiner is requested to address claims 33-50 so as to acknowledge that 50 claims are of record not 26, and to confirm that claims 27-32 which depend from claim 1 are part of the elected group of claims.

Claim Rejections

I. 35 U.S.C. §112, first paragraph

The rejection of claims 1-9 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description and failing to comply with the enablement requirement is respectfully traversed.

The Examiner's understanding of the subject invention is incorrect and unfounded. The present invention as is set forth in amended claim 1 is directed to a method for preparing a library of a plurality of mutant polynucleotides by the substitution of three consecutive nucleotides at a random position of a target DNA. In this regard, the Examiner's attention is invited to the fact that, owing to the

amendment to claim 1 as set forth above, the transposon was limited to "Tn7" employed in the Examples, and the term "multiple" has been deleted.

The term "random" used in the present invention means that the substitution of the nucleotides occurs in any site of the target DNA, not in a defined position or predetermined site.

Briefly, the method for preparing a library of mutant polynucleotides according to the present invention comprises the following steps:

First, transposon Tn7 is inserted into a random position of a target DNA and the transposon is removed from the DNA construct to obtain a library of linearized DNA constructs containing the target DNA cut in one position. Then, three consecutive nucleotides of the target DNA is removed and three consecutive substitutive nucleotides having any nucleotide sequence are inserted in place of the deleted nucleotides by the insertion and removal of DNA cassettes in the cut position of the target DNA, thereby providing a library of mutant polynucleotides having substitutive nucleotides at random positions of the target DNA.

The inventive mutagenesis method is different from the conventional point mutation techniques such as error-prone PCR or chemical mutagenesis in that it changes one or two codons of target DNA by substituting three consecutive nucleotides of the target DNA. However, the inventive method and such existing mutagenesis techniques have in common a feature of providing a random mutation

library of a target DNA. The resulting library may contain mutants having unchanged or deteriorated properties, as well as those having desired (improved) properties. The mutants having desired properties can be obtained from the library by screening or selection procedure. The preparation of the library of mutated polynucleotides by random mutagenesis and the isolation of mutants having desired properties by screening or selecting from the library is universally applicable to all random mutagenesis techniques.

Accordingly, any double stranded DNA used in a conventional mutagenesis method may also be used as the target DNA of the inventive mutagenesis method. For instance, there have been reported mutants of various target proteins, e.g., enzymes, antibodies, antigens, binding proteins, hormones, cytokines and plasma proteins, developed by a conventional mutagenesis method. This is described in the references listed on page 15, lines 5 to 22 of the specification of the subject application which is of record.

It is known to those skilled in the art that random mutagenesis techniques can be universally applied to any target DNA irrespective of its specific nucleotide sequence, length, encoded proteins, or desired property.

In this regard, Applicant has enclosed herewith a Declaration executed by Si-Hyoung LEE, one of the co-inventors, in accordance with 37 CFR 1.132, to0 demonstrate that the inventive method is also applicable to another DNA, i.e., DNA encoding phytase. Accordingly, the application and claims clearly enable one skilled

in the art to practice the invention and therefore, the rejection of the claims as failing to comply with the enablement requirement should be withdrawn.

II. 35 U.S.C. §112, second paragraph

The rejection of claims 1-9 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is respectfully traversed.

The amendments to claims 1 and 3 are believed to overcome any indefiniteness in the claims and hopefully to overcome the misunderstanding of the invention which has apparently led to the rejection of the claims under 35 USC 112 first and second paragraphs.

Claim Rejections - 35 U.S.C. §103

The rejection of claims 1- 9 of the subject application under 35 U.S.C. §103(a) as being unpatentable over Hayes et al. (Cancer Research, 60, pp2411-18 (2000)) in view of Short (US 20040077090) is respectfully traversed.

1) Critical Feature of the Present Invention

Claims 1-9 of the present invention are directed to a method for preparing a library of a plurality of mutated polynucleotides by substituting three consecutive nucleotides at a random position of a target DNA for three consecutive nucleotides which have been removed. This is a critical step in the subject invention. The executed Declaration under 37 CFR 1.132, which is attached hereto,

demonstrates that the method of the present invention is a double stranded target applicable to any DNA irrespective of specific nucleotide sequence length, encoded proteins or property.

2) Comparison with the References cited by the Examiner

By way of review, Hayes et al. disclose a method of pentapeptide scanning mutagenesis technique whereby 5-amino acid insertions are introduced at random in a target protein. Hayes also teaches at page 2415 to 2416 a site-directed mutagenesis for making a single amino acid substitution on the target site.

Short (US 20040077090) teaches at paragraph [1164] to [1178] a saturation mutagenesis which introduces point mutations into a polynucleotide. Further, it discloses at paragraph [1169] the use of a degenerate triplet and explains why it is advantageous for several reasons.

The Examiner has alleged that it would have been obvious to one of ordinary skill in the art to use a three-nucleotide substitution in the method taught by Hayes for the advantages taught by Short. Further, the Examiner also alleges that it would be within one of ordinary skill in the art to pick and choose the number of substitutions since the prior art teaches the substitution of one to five amino acids.

However, the Examiner's attention is invited to the fact that Hayes et al. does not teach or suggest the substitution of three consecutive nucleotides at a

random position of a target DNA for three nucleotides which have been removed, which is essential to the method of the subject invention.

Specifically, for the functional assays for BRCA1 COOH-terminus, Hayes et al. used four complementary and independent strategies: (1) error-prone PCR mutagenesis, (2) pentapeptide insertion mutagenesis, (3) site-directed mutagenesis, and (4) deletion analysis. The pentapeptide insertion mutagenesis always results in the 15-bp insertion in the target DNA, and, if the target DNA is a protein-encoding sequence, this will result in a 5-amino acid insertion at random in the target protein. Further, site-directed mutagenesis results in mutations at a specific site of the target gene. Hayes et al. conducted site-directed mutagenesis by conventional "Quick-Change method" as clearly described in page 2412, left column, not by the combined use of pentapeptide insertion mutagenesis.

As discussed above, Hayes et al. describes the techniques of site-directed mutagenesis and pentapeptide insertion mutagenesis as independent techniques. There is no indication or suggestion in Hayes et al. to combine the techniques for the substitution of three consecutive nucleotides at a random position of the target DNA.

The cited reference, Short, teaches only a saturation mutagenesis method employing a degenerate triplet.

Accordingly, even if the saturation mutagenesis method of Short is combined with the site-directed mutagenesis or the pentapeptide insertion mutagenesis disclosed by Hayes et al., this does not lead one skilled in the art to the preparation of a library of mutated polynucleotides by substituting three consecutive nucleotides at a random position of a target DNA.

The method of the present invention has the following advantages over conventional mutagenesis methods:

The inventive mutagenesis method is more economical than the site-directed mutagenesis method or the saturated mutagenesis method using oligonucleotides, because there is no need to synthesize every mutagenic oligonucleotides specific for each site of the target DNA. Further, since the inventive mutagenesis method does not require a mutagenic oligonucleotide to be bound to the target DNA, it can be easily used without the exact information on the nucleotide sequence of the target DNA.

Accordingly, it is submitted that the prior art documents cited by the Examiner, either alone or in combination, fail to render obvious the present invention.

CONCLUSION

Reconsideration and allowance of claims 1-9 and 27-32 is respectfully solicited.

Respectfully submitted
Attorney for applicants,

Dated: March 7, 2006

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CERTIFICATE OF MAILING

I hereby certify that this Response is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on March 8, 2006.

Audrey De Souza (Typed or printed name of person mailing paper or fee)

Audrey A. de Souza (Signature of person mailing paper or fee)